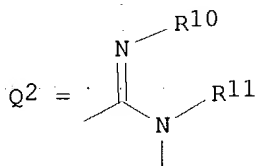
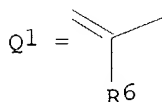
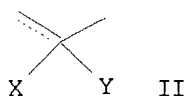
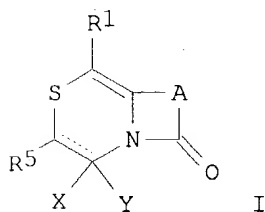


L6 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:888746 HCAPLUS
 DOCUMENT NUMBER: 138:4599
 TITLE: Preparation of fused imidazolidine derivatives as inhibitors of **cartilage** matrix degradation
 INVENTOR(S): Funabashi, Yasunori; Takizawa, Masayuki; Morimoto, Shinji; Notoya, Kohei
 PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
 SOURCE: PCT Int. Appl., 940 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092606	A1	20021121	WO 2002-JP4640	20020514
WO 2002092606	C1	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2003034691	A2	20030207	JP 2002-139642	20020515
PRIORITY APPLN. INFO.:		JP 2001-144608 A 20010515		
OTHER SOURCE(S):		MARPAT 138:4599		
GI				



AB The title compds. I [R₁ = (S)_nR₂, etc.; n = 0 - 2; R₂ = H, (un)substituted

hydrocarbon, etc.; R5 = H, (un)substituted hydrocarbon, etc.; the moiety represented by II in I is Q1, etc.; R6 = H, (un)substituted hydrocarbon, etc.; A = Q2, etc.; R10 = H, ZR15, etc.; Z = SO2, etc.; R15 = (un)substituted hydrocarbon, etc.; R11 = H, (un)substituted hydrocarbon] are prepared A process for preparing I is disclosed. Comps. of this invention in vitro at 0.1 μ M gave 20% to 55% inhibition of MMP-13 production Formulations are given.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:490169 HCAPLUS

DOCUMENT NUMBER: 137:277009

TITLE: Effect of **proteoglycan** on experimental colitis

AUTHOR(S): Majima, Mitsuo; Takagaki, Keiichi; Sudo, Shin-ichiro;

Yoshihara, Syuichi; Kudo, Yoshiaki; Yamagishi, Shohei

CORPORATE SOURCE: Kakuhiro Co. Ltd., Aomori, 030-8543, Japan

SOURCE: International Congress Series (2001), 1223(New

Developments in Glycomedicine), 221-224

CODEN: EXMDA4; ISSN: 0531-5131

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of **proteoglycan** (PG) on colitis was examined in animal expts. using mice. The PG used was extracted from nasal **cartilage** of salmon head with 4% **acetic acid** and prepared by precipitation with ethanol followed by dialysis. The PG contained about 7% protein, and had a mol. mass of 344 kDa on SDS/PAGE. The glycosaminoglycan (GAG) sugar chains of the PG were composed of hexosamine, uronic acid and sulfate at a molar ratio of 1.0:1.0:0.7. The mice were divided into a control group and an administration group. The control group was given free access to drinking water containing dextran sulfate sodium salt (DSS) to induce colitis. On the other hand, the administration group was given free access to drinking water containing DSS and PG. Then, the time course of survival rates in both groups were measured. In the administration group, the survival rate increased significantly in comparison with that of the control group. The difference in the survival rates indicated that the onset of mouse colitis induced by DSS was inhibited by administration of the PG.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:157148 HCAPLUS

DOCUMENT NUMBER: 136:163703

TITLE: A method for extraction and purification of **cartilage** type **proteoglycan**

INVENTOR(S): Takagaki, Keeichi

PATENT ASSIGNEE(S): Kakuhiro Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 8 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 1182209 A2 20020227 EP 2001-117771 20010801
EP 1182209 A3 20030205

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

JP 2002069097 A2 20020308 JP 2000-251071 20000822
US 2002045735 A1 20020418 US 2001-916250 20010730
CN 1439663 A 20030903 CN 2002-104684 20020220

PRIORITY APPLN. INFO.: JP 2000-251071 A 20000822

AB The present invention relates to a new method for extraction and purification
of

cartilage type **proteoglycan**, and is to provide a method
for extraction of crude **proteoglycan** characterized by the use of acid
as eluting solvent of **cartilage**.

L6 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:420949 HCAPLUS

DOCUMENT NUMBER: 133:73860

TITLE: Preparation of 2-(4-bromo or 4-iodo
phenylamino)benzoic acid derivatives as MEK inhibitors

INVENTOR(S): Dudley, David Thomas; Flory, Craig Mason; Saltiel,
Alan Robert

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035436	A2	20000622	WO 1999-US29783	19991215
WO 2000035436	A3	20011018		

W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE,
HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG,
MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ,
VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2346448 AA 20000622 CA 1999-2346448 19991215

EP 1143957 A2 20011017 EP 1999-966278 19991215

EP 1143957 A3 20020227

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

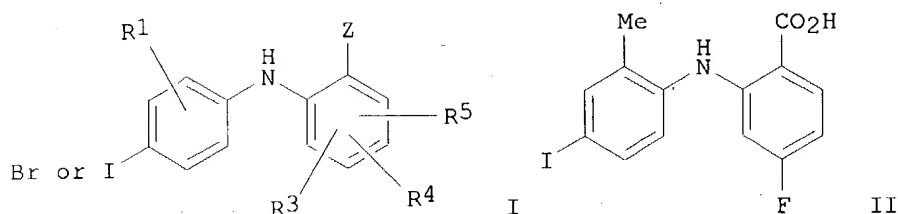
PRIORITY APPLN. INFO.: US 1998-112544P P 19981216

US 1999-164651P P 19991110

WO 1999-US29783 W 19991215

OTHER SOURCE(S): MARPAT 133:73860

GI



AB The title compds. (I) [wherein R1 = H, OH, alkyl, alkoxy, halo, CF3, or CN; R3-R5 = independently H, OH, halo, CF3, alkyl, alkoxy, NO2, CN, or (O or NH)m-(CH2)n-R9, where R9 = H, OH, CO2H, or NR10R11; m = 0 or 1; n = 0-4; R10 and R11 = H, alkyl, or taken together with the N to which they are attached form a 3-10 membered ring; Z = CO2R7, tetrazolyl, CONR6R7, CONHNR10R11, or CH2OR7; R6 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, acyl, (hetero)aryl, or taken together with the N to which they are attached form a 3-10 membered ring, etc.] were prepared by standard or combinatorial synthetic methods involving the addition of halobenzoic acids to haloanilines and optional reduction or amidation of the acid. For example, treatment of 2-amino-5-iodotoluene in THF with LDA in THF/heptane/ethenylbenzene solution, followed by addition of 2,4-difluorobenzoic acid in THF afforded II. In assays against type II collagen induced arthritis in mice and monoarticular arthritis in rats, I showed potent anti-arthritic activity. I inhibited IL-1 induced stromelysin production in rabbit synovial fibroblast cell cultures with IC50 from 9 nM to 192 nM. Interleukin 1-alpha stimulated **cartilage** degradation was reduced by up to 75% in New Zealand white rabbits upon administration of I. Thus, I are potent MEK inhibitors useful in the prevention and treatment of rheumatoid arthritis or osteoarthritis.

L6 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:205318 HCAPLUS

DOCUMENT NUMBER: 130:267212

TITLE: Biphenyl-derived substituted cycloalkanecarboxylic acid derivatives and analogs as matrix metalloprotease inhibitors

INVENTOR(S): Kluender, Harold Clinton Eugene; Bullock, William Harrison; Dixon, Brian Richard; Schneider, Stephan; Vanzandt, Michael Christopher; Wilhelm, Scott McClelland; Wolanin, Donald John

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S., 102 pp., Cont. of U.S. Ser. No. 463,471, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

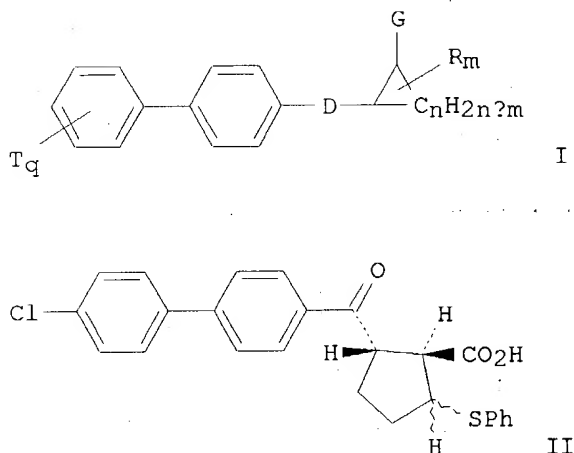
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5886022	A	19990323	US 1997-866568	19970530
PRIORITY APPLN. INFO.:			US 1995-463471	19950605

OTHER SOURCE(S):
GI

MARPAT 130:267212



AB The invention discloses inhibitors for matrix metalloproteases (MMPs), pharmaceutical compns. containing the inhibitors, and a process for using them to treat a variety of physiol. conditions. The claimed compds. have the generalized formula I [wherein each T = halo, alk(en/yn)yl, (CH₂)_pQ, etc.; Q = aryl, heteroaryl, cyano, CHO, NO₂, etc.; p = 0-4; q = 0-2; D = CO, CH(OH), C:NOH, C:S; n = 2 or 3; R = alk(en/yn)yl, aralk(en/yn)yl; G = CO₂H, alkoxycarbonyl, (di)(alkyl)carbamoyl, or amino acid residues bound at N via a CO linker; m = 0-2]. Approx. 250 compds. including both I and many acyclic carboxylic acid analogs were prepared. For instance, Friedel-Crafts acylation of 4-chlorobiphenyl by 1-cyclopentene-1,2-dicarboxylic anhydride, followed by lithiation/reprotonation to effect double-bond isomerization, and Michael addition of thiophenol to the double bond, gave 2 diastereomers of title compound II. The trans,trans isomer of II was the most active diastereomer, with IC₅₀ values as follows: MMP-3 14-47 nM, MMP-9 56 nM, and MMP-2 4 nM.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 11, HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:742237 HCAPLUS

DOCUMENT NUMBER: 130:17266

TITLE: Chemical cleaning of biological material

INVENTOR(S): Abraham, Ginger A.; Carr, Robert M., Jr.; Kemp, Paul D.; Mercer, Ryan; Baker, Linda

PATENT ASSIGNEE(S): Organogenesis Inc., USA

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849969	A1	19981112	WO 1998-US9432	19980508
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5993844	A	19991130	US 1997-853372	19970508
AU 9872947	A1	19981127	AU 1998-72947	19980508
AU 736312	B2	20010726		
BR 9809216	A	20000627	BR 1998-9216	19980508
EP 1018979	A1	20000719	EP 1998-920349	19980508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002510995	T2	20020409	JP 1998-548536	19980508
NO 9905372	A	19991103	NO 1999-5372	19991103
MX 9910251	A	20000630	MX 1999-10251	19991108
US 6599690	B1	20030729	US 1999-450577	19991130
US 2004005703	A1	20040108	US 2003-615623	20030708
PRIORITY APPLN. INFO.:			US 1997-853372	A2 19970508
			WO 1998-US9432	W 19980508
			US 1999-450577	A1 19991130

AB Collagenous tissues are treated to remove noncollagenous components such as cells, cellular debris, and other extracellular matrix components such as **proteoglycans** and glycosaminoglycans, normally found in native tissues, by treatment of the tissue with alkali, chelating agents, acids, and salts while controlling the amount of swelling and dissoln. so that the resultant collagen matrix retains its structural organization, integrity, and bioremodelable properties. The process circumvents the need to use detergents and enzymes, which detrimentally affect the cell compatibility, strength, and bioremodelability of the collagen matrix. The collagenous tissue matrix is used for implantation, repair, or similar use in a mammalian host. Thus, pig small intestine was mech. stripped to remove fat, muscle, and mucosal layers from the tunica submucosa. The submucosa was then shaken successively at .apprx.200 rpm with (a) 100 mM tetra-Na EDTA/10 mM NaOH for 18 h, (b) 1M HCl/1M NaCl for 6-8 h, (c) 1M NaCl/10 mM phosphate-buffered saline for 18 h, (d) 10 mM phosphate-buffered saline for 2 h, and (e) sterilized water for 1 h. Treated tissue samples appeared free of cells and cellular debris.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:534889 HCAPLUS

DOCUMENT NUMBER: 129:161412

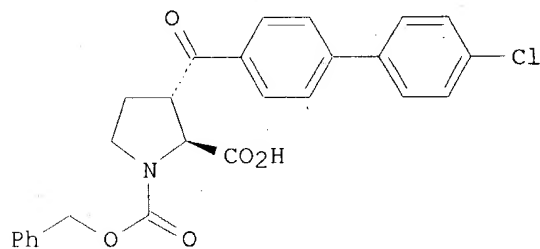
TITLE: Derivatives of substituted 4-biarylbutyric acid as matrix metalloprotease inhibitors

INVENTOR(S): Kluender, Harold Clinton Eugene; Benz, Guenter Hans
Heinz Herbert; Brittelli, David Ross; Bullock, William
Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard;
Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt,
Michael Christopher; Wolanin, Donald John; Wilhelm,
Scott M.

PATENT ASSIGNEE(S): Bayer Corporation, USA
 SOURCE: U.S., 109 pp., Cont.-in-part of U.S. Ser. No. 339,846.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5789434	A	19980804	US 1995-539409	19951106
CA 2201863	AA	19960523	CA 1995-2201863	19951109
CN 1163604	A	19971029	CN 1995-196209	19951109
CN 1121376	B	20030917		
HU 78083	A2	19990830	HU 1998-233	19951109
PT 790974	T	20021129	PT 1995-940572	19951109
ES 2181803	T3	20030301	ES 1995-940572	19951109
ZA 9509647	A	19970814	ZA 1995-9647	19951114
TW 413675	B	20001201	TW 1995-84112045	19951114
US 5874473	A	19990223	US 1997-864666	19970528
US 5886024	A	19990323	US 1997-865325	19970528
US 5854277	A	19981229	US 1997-865639	19970530
US 5859047	A	19990112	US 1997-866798	19970530
US 5861427	A	19990119	US 1997-866679	19970530
US 5861428	A	19990119	US 1997-866680	19970530
US 5886043	A	19990323	US 1997-866778	19970530
US 6166082	A	20001226	US 1998-57679	19980409
PRIORITY APPLN. INFO.:			US 1994-339846	A2 19941115
			US 1995-462729	B1 19950605
			US 1995-463490	B1 19950605
			US 1995-463580	B1 19950605
			US 1995-463794	B1 19950605
			US 1995-464253	B1 19950605
			US 1995-465626	B1 19950605
			US 1995-539409	A 19951106

OTHER SOURCE(S): MARPAT 129:161412
 GI



I

AB Matrix metalloprotease (MMP) inhibitors TxA-B-D-E-G [I; T = halo, haloalkyl, alkynyl, (un)substituted alkyl or alkenyl; x = 0, 1, 2; A, B = aromatic or heteroarom. ring; D = CO, CH(OH), CH2, C:NOH, C(S); E = substituted carbon chain; G = PO3H2, CO2H, CO2NH2, 5-tetrazolyl, etc.] and their pharmaceutically acceptable salts were prepared. In particular, I [A = C6H4; B = 1,4-C6H4; E = certain substituted THF, tetrahydrothiophene, or

pyrrolidine divalent radicals] with MMP inhibitory activity, and their pharmaceutically acceptable salts, are claimed. For instance, claimed title compound II was prepared from L-pyroglutaminol in 9 steps. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. For instance, II had corresponding IC50 values of 103, 381, and 35 nM. I inhibited tumor growth and metastasis in animal models, and inhibited **cartilage** lesions in a guinea pig model of osteoarthritis.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:702288 HCAPLUS

DOCUMENT NUMBER: 127:329857

TITLE: Reaction of hypochlorous acid with bovine nasal **cartilage** comparison to pig articular **cartilage**

AUTHOR(S): Schiller, Jurgen; Arnhold, Jurgen; Zachaus, Annett; Arnold, Klaus

CORPORATE SOURCE: Medizinische Fakultät, Universität Leipzig, Leipzig, D-04103, Germany

SOURCE: Zeitschrift fuer Naturforschung, C: Biosciences (1997), 52(9/10), 694-701

CODEN: ZNCBDA; ISSN: 0341-0382

PUBLISHER: Verlag der Zeitschrift fuer Naturforschung

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The action of NaOCl on bovine nasal **cartilage** was studied by 1H-NMR spectroscopy to model degradation processes of **cartilage** caused by neutrophil-derived hypochlorous acid. Nasal **cartilage** was chosen as a mean of comparison because it differs from articular **cartilage** in its composition. It contains some more **proteoglycans**, i.e. polymeric carbohydrates and less collagen than articular **cartilage**. This is important for studying the influence of hypochlorous acid on **cartilage** components (collagen and polysaccharides). **Cartilage** samples were incubated at 37° with phosphate buffer in the presence or absence of NaOCl. Supernatants were collected and assayed by NMR-spectroscopy. In the presence of pure phosphate buffer, the supernatants of bovine nasal **cartilage** were less rich in low mol. mass metabolites (e.g. amino acids, lactate) than articular **cartilage**. However, intense signals for highly mobile N acetyl groups of **cartilage** polysaccharides were detectable in nasal **cartilage**. NaOCl caused an increase in signals for acetate and formate. Signals for N-acetyl groups rose only during the first 25 min of incubation with NaOCl. Then, their concentration decreased markedly. These changes were related to an enhanced release of chondroitinsulfate from nasal **cartilage**.

L6 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:476807 HCAPLUS

DOCUMENT NUMBER: 125:142275

TITLE: Substituted 4-biarylbutyric or 5-biarylpentanoic acids and derivatives as matrix metalloprotease inhibitors

INVENTOR(S): Kluender, Harold Clinton Eugene; Benz, Guenter Hans Heinz Herbert; Brittelli, David Ross; Bullock, William Harrison; Combs, Kerry Jeanne; Dixon, Brian Richard; Schneider, Stephan; Wood, Jill Elizabeth; Vanzandt,

PATENT ASSIGNEE(S): Michael Christopher; et al.
 SOURCE: Bayer A.-G., USA
 PCT Int. Appl., 263 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615096	A1	19960523	WO 1995-US14002	19951109
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2201863	AA	19960523	CA 1995-2201863	19951109
AU 9641975	A1	19960606	AU 1996-41975	19951109
AU 702317	B2	19990218		
EP 790974	A1	19970827	EP 1995-940572	19951109
EP 790974	B1	20020814		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9509686	A	19970930	BR 1995-9686	19951109
CN 1163604	A	19971029	CN 1995-196209	19951109
CN 1121376	B	20030917		
JP 10509146	T2	19980908	JP 1995-516097	19951109
HU 78083	A2	19990830	HU 1998-233	19951109
RU 2159761	C2	20001127	RU 1997-110108	19951109
EE 3435	B1	20010615	EE 1997-210	19951109
PL 183549	B1	20020628	PL 1995-320285	19951109
AT 222230	E	20020815	AT 1995-940572	19951109
PT 790974	T	20021129	PT 1995-940572	19951109
ES 2181803	T3	20030301	ES 1995-940572	19951109
ZA 9509647	A	19970814	ZA 1995-9647	19951114
FI 9702062	A	19970714	FI 1997-2062	19970514
NO 9702220	A	19970714	NO 1997-2220	19970514
US 5874473	A	19990223	US 1997-864666	19970528
US 5886024	A	19990323	US 1997-865325	19970528
US 5854277	A	19981229	US 1997-865639	19970530
US 5859047	A	19990112	US 1997-866798	19970530
US 5861427	A	19990119	US 1997-866679	19970530
US 5861428	A	19990119	US 1997-866680	19970530
US 5886043	A	19990323	US 1997-866778	19970530
PRIORITY APPLN. INFO.:			US 1994-339846	A 19941115
			US 1995-462729	B1 19950605
			US 1995-463490	B1 19950605
			US 1995-463580	B1 19950605
			US 1995-463794	B1 19950605
			US 1995-464253	B1 19950605
			US 1995-465626	B1 19950605
			WO 1995-US14002	W 19951109

OTHER SOURCE(S): MARPAT 125:142275

AB Matrix metalloprotease inhibitors TxA-B-D-E-G [Tx = substituent such as halo, C1-C10 alkyl, or cyanoalkenyl; x = 0, 1, 2; A, B = aromatic or

heteroarom. ring; D = CO, CH(OH), CH₂, C:NOH, C(S); E = substituted carbon chain; G = PO₃H₂, CO₂H, CO₂NH₂, etc.] and their pharmaceutically acceptable salts were prepared. Thus, (S)-γ-oxo-4'-(pentyloxy)-α-(3-phenylpropyl)-[1,1'-biphenyl]-4-butanoic acid (86) was prepared via alkylation of di-Et (3-phenylpropyl)malonate with 2,4'-dibromoacetophenone, followed by saponification-monodecarboxylation, reaction with 4-methoxybenzeneboronic acid, Me ether cleavage, and O-pentylation. The synthesized compds. (444) were assayed for inhibition of MMP-3, MMP-9, and MMP-2. Using compds. such as 86, the number of tumor metastases was decreased between 38 and 49% as compared to the control. The title compds. were also assayed for inhibition of **cartilage** lesions in a guinea pig model of osteoarthritis.

L6 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:209947 HCAPLUS

DOCUMENT NUMBER: 110:209947

TITLE: Effects of chondroitinase-ABC on **proteoglycans** and swelling properties of fibrocartilage in bovine flexor tendon

AUTHOR(S): Koob, Thomas J.

CORPORATE SOURCE: Dep. Biol., Univ. New Mexico, Albuquerque, NM, 87131, USA

SOURCE: Journal of Orthopaedic Research (1989), 7(2), 219-27
CODEN: JOREDR; ISSN: 0736-0266

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fibrocartilaginous regions of bovine deep flexor tendon were treated with chondroitinase-ABC and trypsin to extract **proteoglycans** from the extracellular matrix and thereby investigate the contribution of **proteoglycan** and collagen organization to tissue material properties. Chondroitinase-ABC digestion of tendon specimens for 24 h resulted in extraction of 60% of the tissue glycosaminoglycans and leaching of the degraded large **proteoglycan** from the tissue residue. The totally degraded core protein of the small dermatan sulfate **proteoglycan** remained with the tissue residue, indicating that it is specifically associated with the tissue residue and that this association is not dependent on the glycosaminoglycan chains. Treatment of residues with trypsin after chondroitinase-ABC digestion depleted the specimens of **proteoglycan**. Bulk swelling tests on enzyme-extracted specimens showed that the distinct swelling properties of the fibrocartilaginous regions of the distal flexor tendon could be partially accounted for by elevated levels of **proteoglycan**. Swelling tests also showed that the distinct collagen organization of this region contributes significantly to the tissue's material properties. Apparently, the fibrocartilaginous organization and composition of the articulating layer of distal tendon are adapted for mech. requirements unique to this site, which receives compressive and frictional loads in addition to tensile loads.

L6 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1973:54498 HCAPLUS

DOCUMENT NUMBER: 78:54498

TITLE: Structural studies on **cartilage** collagen employing limited cleavage and solubilization with pepsin

AUTHOR(S): Miller, Edward J.

CORPORATE SOURCE: Med. Cent., Univ. Alabama, Birmingham, AL, USA

SOURCE: Biochemistry (1972), 11(26), 4903-9
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Insol. **cartilage** collagen was prepared as the residue from the sternal **cartilages** of 10-week-old chickens by exhaustive extraction with M NaCl at neutral pH and 0.5 M **acetic acid**. The extraction procedures were totally ineffective in solubilizing **cartilage** collagen but were useful as a means of removing **proteoglycan** components of the tissue. Amino acid analyses of the insol. **cartilage** collagen residue revealed an amino acid composition closely resembling that of purified $\alpha 1(\text{II})$ chains. Characterization of the CNBr cleavage products derived from insol. **cartilage** collagen indicated that they are, for the most part, qual. identical with those previously observed in CNBr digest of $\alpha 1(\text{II})$ prepared from soluble **cartilage** collagen. However, 2 addnl. CNBr peptides (designated peptides 14 and 15) comprising a total sequence of 21 amino acids derived from a nonhelical region of the **cartilage** collagen mol. were identified. Incubation of insol. **cartilage** collagen in 0.5 M **acetic acid** containing pepsin (ratio of collagen: enzyme = 10:1) at 4° for 18 hr solubilized 60-70% of the collagen. Characterization of the pepsin-solubilized **cartilage** collagen with respect to chain composition, mol. weight of the component α chains and CNBr cleavage products of the chains indicated that the collagen was solubilized as monomeric mols. of the chain composition, $\{\alpha 1(\text{II})\}_3$, and that the proteolytic activity of pepsin on the native **cartilage** collagen mol. is confined to relatively short sequences represented by the CNBr peptides, 1,4,14,15, and the CO₂H-terminal portion of peptide 7. These results indicating that the cited sequences do not participate in collagen helix formation and that they are localized at the extremities of the $\alpha 1(\text{II})$ chains comprising the **cartilage** collagen mol. have been used, in conjunction with addnl. data on the location of peptides 1 and 4, to establish that the order of the CNBr peptides in the carboxy-terminal region of the $\alpha 1(\text{II})$ chain is: 7-14-15. These results further indicate that failure to detect peptides 14 and 15 in the CNBr cleavage products of $\alpha 1(\text{II})$ prepared from soluble **cartilage** collagen resulted from nonspecific proteolytic activity during extraction and purification of the collagen. It is proposed that the mechanism whereby the proteolytic activity of pepsin alters the solubility properties of **cartilage** collagen involves, at least in part, the degradation of the sequence represented by peptide 4, thus effectively eliminating a site of intermol. cross-linking known to occur in this sequence.